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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,033	08/09/2005	Jean-Pierre Vors	P/3610-57	6764

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EXAMINER	
ZAREK, PAUL E	
ART UNIT	PAPER NUMBER
1628	
MAIL DATE	DELIVERY MODE
01/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,033	VORS ET AL.	
	Examiner	Art Unit	
	Paul Zarek	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5,7-11,14-17,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,7-11,14-17,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/01/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claim 16 has been amended by the Applicant in correspondence filed on 09/24/2009. Claims 2-5, 7-11, 14-17, 20, and 21 are currently pending. This is the second Office Action on the merits of the claim(s) following for a request for continued examination.

RESPONSE TO ARGUMENTS

2. Claims 16, 2-5, 14, and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Charles, et al. (International Application No. WO 00/46184). Applicants traversed this rejection on the grounds that Charles, et al., does not contemplate treating *Candida albicans* or *Aspergillus fumigatus* infections in humans and that the disclosure of Charles, et al., teaches only treating Ascomycetes in general, but not *C. albicans* or *A. fumigatus* in particular. After careful consideration, Examiner finds Applicants' arguments persuasive. The rejection of Claims 16, 2-5, 14, and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Charles, et al., is withdrawn.

3. Claims 16, 5, 7-11, and 17, 20, and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Charles, et al., in view of Bennett (Goodman & Gillman, The Pharmaceutical Basis of Therapeutics, 10th ed., 2001). Applicants traversed this rejection on the grounds that Charles, et al., do not teach or render obvious treating *C. albicans* or *A. fumigatus* in humans (see above). Applicants further assert that Charles, et al., do not teach combining compound I with another antifungal compound (compound II), having a synergistic effect with compound II, or

further comprising a pharmaceutical excipient. Applicants point to the examples in the instant specification as evidence of unexpected synergy. Respectfully, Examiner does not find Applicants' arguments persuasive.

4. Charles, et al., discloses that antifungal compounds possessing the same number and identity of substituents claimed in the instant invention (pg 1, line 16 through pg 3, line 22), and explicitly discloses compounds 364 and 365, which correspond to compounds I.1 and I.2 (both in instant Claim 17). Charles, et al., contemplate treating fungal infestations in domestic and farm animals (pg 13, lines 32-33). Charles, et al., further teach that the compounds disclosed therein may be active against "general pathogens of . . . Ascomycete" (pg 10, lines 9-11). It is noted that both *C. albicans* and *A. fumigatus* belong to the phylum Ascomycota, and are thus considered Ascomycetes. Examiner appreciates that Ascomycetes encompass a diverse array of fungi. However, Charles, et al., demonstrates that the compounds contained therein are effective against multiple species of ascomycota: *Erysiphe graminis, Pyricularia oryzae,* and *Leptosphaeria nodorum*. These ascomycetes belong to subphylum Pezizomycotina, the same subphylum as *A. fumigatus*, yet belong to different classes (Leotiomycetes, Sordariomycetes, and Dothideomycetes, respectively). Furthermore, Charles, et al., is not the only art disclosing that a single class of compounds is effective against a broad array of ascomycetes. Indeed, Nieto-Roman, et al (International Application no. WO 01/049666; English equivalent: US PreGrant Publication no. 2003/0191113), teach that a single class of compounds, which are similar to but not obvious over the claimed compounds, is effective against numerous fungi, many of which are ascomycetes (paragraphs 0215-0234), including *C. albicans* and *A. fumigatus* (paragraph 0248). McGinnis and Pasarell (Journal of Clinical Microbiology, 1998) discloses that itraconazole is

effective against a wide variety of ascomycetes as well (Table I). Thus, one of ordinary skill in the art would reasonably expect that the compounds discloses in Charles, et al., would be effective against a wide variety of fungi, including *C. albicans* and *A. fumigatus*.

5. Charles, et al., discloses that the compounds disclosed therein would be effective to treat fungal infections of domestic or farm animals. It would be expected that such anti-fungal medication would also be effective for humans because it would be reasonably expected the herein claimed compounds to exhibit the same antifungal activity against the herein claimed pathogens regardless of whether the host is human or not.

6. Applicants do not deny that fluconazole and itraconazole are well known for the treatment of *C. albicans* and *A. fumigatus* infections. Combining two compounds known to do the same thing into a composition to treat the same disease is not a patentably distinguishing feature of an invention (*In re Kerkhoven*). Instead, Applicants contend that the combination of compound I.1 or I.2 with fluconazole or itraconazole (both are encompassed by compound II) demonstrates unexpectedly superior results (i.e. synergy) against candidiasis and aspergillosis. The instant disclosure does not provide sufficient data for the skilled artisan to conclude that Applicants have demonstrated synergy. Applicants point to Table 6 as proof of the alleged unexpected synergism. Examiner respectfully disagrees. Applicants define the "level of interaction" (L.I.) between fluconazole/itraconazole with the claimed compounds as the ratio of the expected effected concentration to the observed concentration. An L.I. of greater than 1.15 is an indication of synergism, a L.I. of less than 0.5 is an indication of antagonism, and an L.I. between 0.5 and 1.0 is an indication of an additive effect, which would be expected. Of the eight conditions disclosed in Table 6, three conditions demonstrate a synergistic effect, three

conditions demonstrate an antagonistic effect, and two demonstrate an additive effect. Such a disclosure is not sufficient to prove drug synergy over the scope of the entire claims.

7. For the above reasons, the rejection of Claims 16, 5-11, 17, 20, and 21 under 35 U.S.C. 103(a) as being unpatentable over Charles, et al., in view of Bennett, is maintained.

8. Below are listed new grounds of rejection that are not necessitated by amendment to the claims. Therefore, this office action is considered **non-final.**

Claim Rejections - 35 USC § 103

9. The text of Title 35, U.S.C. § 103(a) can be found in a prior Office action.

10. Claims 2-4, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charles, et al. (International Application no. WO 00/46184, already of record).

11. Claims 2-4 limit compounds utilized in the method of Claim 16. Compounds I.1 and I.2 read upon these claims. Claims 14 and 15 limit infection to be treated to be caused by *C. albicans* and *A. fumigatus* respectively.

12. Charles, et al., was described above and previously. Briefly, Charles, et al., disclose that compounds I.1 and I.2 (compounds 364 and 365 in this art) are effective against general pathogens of Ascomycete. Charles, et al., contemplate treating fungal infestations in domestic and farm animals (pg 13, lines 32-33). Charles, et al., do not disclose treating *C. albicans* or *A. fumigatus* infections in humans.

13. Although Charles, et al., only contemplates treating farm and domestic animals, it would be expected that such anti-fungal medication would also be effective for humans because it

would be reasonably expected the herein claimed compounds to exhibit the same antifungal activity against the herein claimed pathogens regardless of the host. Applicants' arguments that one of ordinary skill in the art would not reasonably conclude that the compounds of Charles, et al., would be effective against *C. albicans* or *A. fumigatus* is not persuasive, as both Nieto-Roman, et al. (above), and McGinnis and Pasarell (above) demonstrate that single compounds can be effective against a diverse array of fungi with phylum Ascomycota. Thus, one of ordinary skill in the art would not be "varying all parameters" contained with Charles, et al., but the artisan would reasonably expect that compounds I.1 and I.2 would be effective for the treatment of *C. albicans* and *A. fumigatus* given the disclosure of Charles, et al. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to treat *C. albicans* and *A. fumigatus* infections in humans with compounds I.1 and I.2.

Conclusion

14. Claims 16, 5, 7-11, 17, 20, and 21 remain rejected. Claims 2-4, 14, and 15 are newly rejected.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1628